#AP03

EPROGEN INC

The Use of *NPS*® for Fast On-Line Process Monitoring

NPS® is a breakthrough in fast HPLC. *NPS* is ultra-pure, highly uniform non porous silica spheres which provide the LC chromatographer greatly improved mass transfer and lower detection limits. Coupled with enhanced stability and dramatically reduced solvent usage, *NPS* is the ideal column to meet the ever increasing demands placed on today's analytical labs - Improved productivity at a lower cost.

This paper was originally presented at IFPAC$_{SM}$'96, Jan. 21-24, 1996 in Orlando FL entitled: "On-line HPLC monitoring of a deprotecting process" by Z. Ge, R. Thompson, D. DeTora, T. Maher, P. McKenzie, D. Ellison and J. Crutchfield, Merck Research Laboratories, P.O. Box 2000, Rahway, NJ 07065.

The development of an on-line analysis of the deprotecting step in the synthesis of *indinavir* (an HIV-1 protease inhibitor) was successfully accomplished using the MICRA *NPS* ODS-I 4.6x33 mm column. The usual method for this analysis has been off-line using a porous C-18 column (25cm length) where seven components are monitored including two highly unstable and undesirable intermediates that can be underreported if not rapidly assayed. The total analysis time for this off-line method is one hour including sample preparation. The development of an on-line analysis has eliminated the need for any operator sample handling of the highly corrosive and hazardous samples and reduced the analysis time from one hour to 18 minutes per sample. This has significantly improved sample turnaround time and the collection of data for better process control and optimization.

Figure 1. On-line analysis of typical reaction mixture from the deprotecting step of indinavir synthesis.

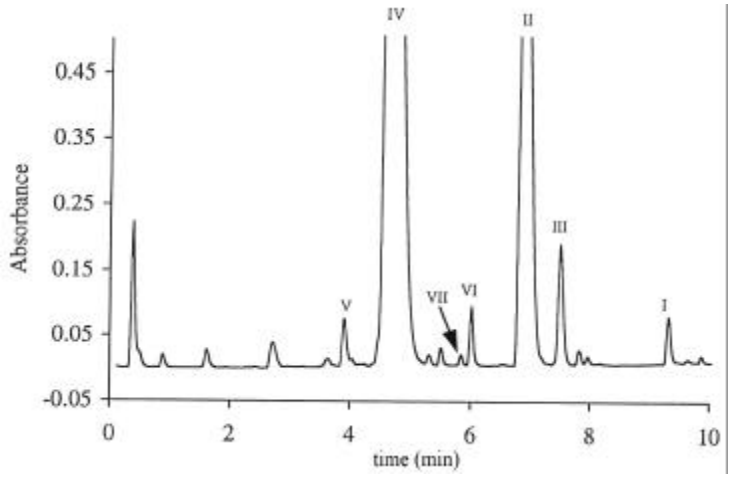
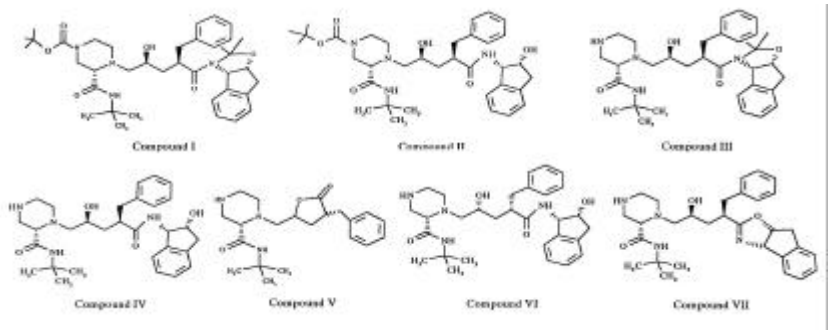


Figure 2. Structures of the compounds of interest



Think small

Think fast

Think *NPS*®

Figure 3. Synthetic mixture on MICRA *NPS* 1.5µm ODS-I

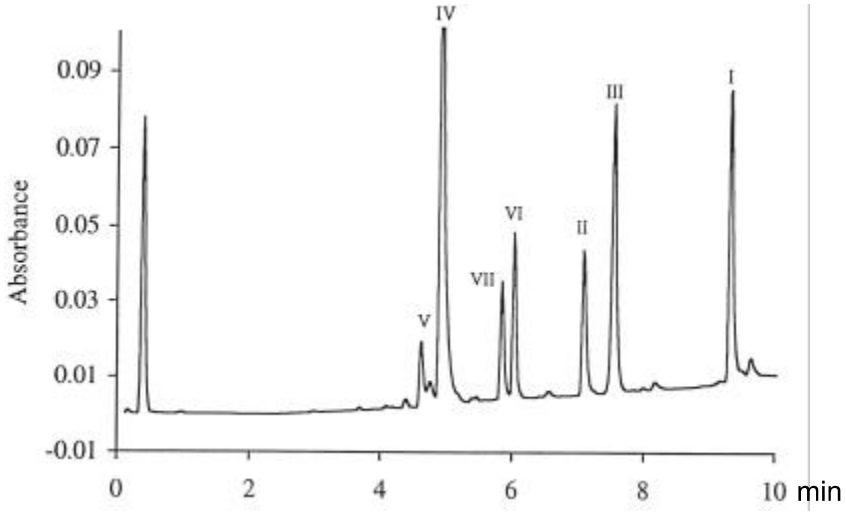
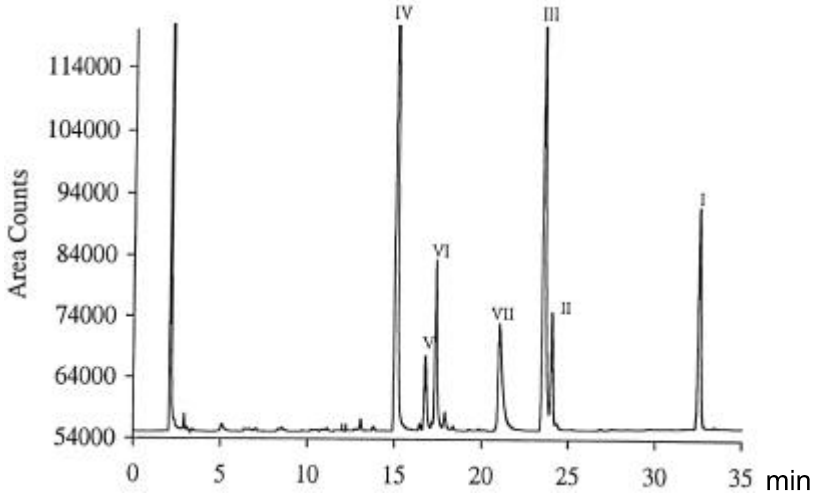


Figure 4. Chromatogram of synthetic mixture on porous ODS-2



Operating Conditions

	MICRA *NPS* ODS-I	Inertsil ODS-2
Column		
Detector/Flow Cell	UV 220 nm	UV 220 nm
Column	1.5 µm, 33x4.6mm ID	5 µm, 250x4.6
Mobile Phase	A: 20mM KH_2PO_4, pH 2.5 B: ACN	A: 2mM KH_2PO_4, 8mM K_2HPO_4, pH 7.5 B: ACN
Gradient	95% A to 55% A in 10 min.	20%B for 3 min, 20% to 80% over 30 min, hold 2 min
Flow Rate	1.0 mL/min	1.0 mL/min
Temperature	Ambient	Ambient
Injection Volume	2µL	20µL
Sample Solvent	50/50 50mM K_2HPO_4/ACN	50/50 10mM K_2HPO_4 pH 7.5/ACN
Run Time	10 minutes	35 minutes
System Void Volume	0.3 mL	2.3 mL

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